REMARKS

Claims 1-7 are pending. Claims 1 and 5 have been amended. Claim 7 is newly added. No new matter has been added by the amended and new claims. Support for the amended claims 1 and 5 is found in the specification p.2, lines 1-8, and Examples 2 and 3, p.8, line 16 to p.9, line 15. Support for new claim 7 is found in the specification p.7, lines 5-8, and Example 4, p.9, lines 16 to p10, line 2.

Rewritten claims appear in the preceding "Amendments" section. Attached hereto is a marked-up version of the changes made to amended claims. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE" and is only included for the Examiner's convenience. Should any discrepancies be discovered, the version presented in the preceding "Amendments" section shall take precedence.

Rejections under 35 USC §102(b)

I. Jacobs (WO 99/55910).

Claims 1, 3, and 4 have been rejected under 35 USC §102(b) as being anticipated by Jacobs (WO99/55910). The Examiner has objected to the use of open language (having) to recite the deletion in the region coding the E3L gene product and hence is not limited to amino acids 184-190 of the E3L gene product. The Applicants respectfully traverse this rejection.

For a claim to be anticipated by a reference, "there must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565

18 USPQ2d 1001, 18 USPQ 2d 1896 (Fed. Cir. 1991). Moreover, a claim is anticipated and fails to meet the requirement of §102 only when a single prior art reference discloses each and every element of the claimed invention. *Lewmar Marine, Inc. v. Barient*, 3 USPQ 2d 1766 (Fed. Cir. 1987).

Claim 1 has been amended to indicate that the expression vector comprising a vaccinia virus comprising an E3L gene having a deletion in amino acids 184-190 of the E3L gene product has reduced pathogenicity in an animal host. The present invention is directed to a recombinant vaccinia virus comprising (1) exogenous DNA and (2) an E3L gene with deletions in the C terminal portion of the E3L gene product. The detailed description of the invention indicates that such a recombinant vaccinia virus allows for viral replication, protein synthesis and interferon-resistance that is indistinguishable from wild-type virus, but has remarkably reduced pathogenicity in mice relative to wild-type vaccinia virus of the same strain (see Example 2 of specification pp.8-9). Furthermore, the resulting recombinant vaccinia viruses of the present invention are useful as vaccines and anticancer agents.

In stark contrast, Jacob is directed towards a method of inducing apoptosis in a cancer cell, using a vaccinia virus vector in which the E3L gene has been deleted or inactivated, comprising a nucleic acid encoding an antisense RNA that is complementary to an mRNA that is specific to a target cell, wherein said nucleic acid is operably linked to a promoter (see Jacobs claims, particularly claims 1 and 14). The E3L gene codes for double-stranded RNA (dsRNA) binding proteins which can inhibit apoptosis (p4 line 25 to p5 line 8). Jacob teaches that deletion of the E3L gene can induce apoptosis. Jacob does not teach an expression vector comprising a

vaccinia virus with reduced pathogenicity in an animal host. In fact, a vaccinia virus that induces apoptosis of host cells, such as that taught by Jacobs, actually teaches away from a reduced pathogenic virus, since increased apoptosis correlates with increased pathogenicity. Therefore, Jacob fails to teach each and every element of the claimed invention. The Applicants submit that one of ordinary skill in the art would be able to clearly distinguish the claims of the present invention from the cited art.

For all the foregoing reasons, Applicants respectfully submit that claims 1, 3, and 4, as amended, cannot be anticipated by Jacobs (WO 99/55910). Therefore, Applicants respectfully request the withdrawal of rejection of claims 1, 3, and 4 under 35 U.S.C. §102 (b).

II. Beattie *et al.*

Claims 1-5 have been rejected under 35 USC §102(b) as being anticipated by Beattie *et al.* ("Beattie I"). The Examiner alleges that Beattie I recites expression vectors comprising a vaccinia virus having a deletion in the E3L region which encompasses the region encoding amino acids 184-190 wherein said vector further comprises exogenous DNA encoding an antigen operably linked to regulatory elements that control expression of said exogenous DNA and compositions comprising the vector and a carrier. The Applicants respectfully disgree.

Beattie I teaches a wild type vaccinia virus, Copenhagen strain, VC-2, in which the E3L gene has been completely deleted. Beattie I suggests that this strain of vaccinia virus does not allow for testing in animals. Deletion of the E3L gene from the Copenhagen VC-2 strain restricts its host-range (Beattie I, p.499, last paragraph; p.504 first paragraph) in comparison to

the wild type strain with the full length E3L gene. Beattie II further teaches that the E3L gene is required for productive replication in Vero, HeLa, and murine L929 cells, but not in chick embryo fibroblasts (see also Beattie *et al.* "Host range restriction of vaccinia virus E3L-specific deletion of mutants" Virus Genes 12:89-94, 1996, Exhibit 1 ("Beattie II")). Vaccinia viruses are considered useful as expression vectors because they have a wide host range (specification, p.1 line 4). In fact, Beattie I teaches away from the use of a vaccinia virus with a deleted E3L gene as an expression vector. A virus strain with a limited host cell range such as that taught by Beattie I would not be desired as a vehicle for expression as claimed in the present invention.

The present invention claims an expression vector comprising a recombinant vaccinia virus which comprises a E3L gene having deletions in the C terminal portion of the E3L gene product. The Applicants submit that Beattie I does not teach one of ordinary skill in the art the present invention.

For all the foregoing reasons, Applicants respectfully submit that claims 1-5, as amended cannot be anticipated by Beattie *et al.* Applicants respectfully request the withdrawal of rejection of claims 1-5 under 35 U.S.C. §102 (b).

The Applicants also request that the objection of claim 6 be withdrawn since it is dependent on an allowable amended base claim.

Objection of Oath

The Examiner has objected to the Declaration because it was not signed by one of the inventors. The Applicants submit herewith a properly executed Supplemental Combined Declaration and Power of Attorney. A faxed copy of the signed page also contains corrections to the address which have been initialed. The address is 3374 Daley Center Drive, #1710, San Diego CA, 92123.

CONCLUSION

Based on the foregoing remarks, Applicants submit that the present application is in condition for allowance. A Notice of Allowance is respectfully requested.

Respectfully submitted,

Louis S. Sorell
Patent Office Reg. No. 32,439

Alicia A. Russo
Patent Office Reg. No. 46,192

Attorneys for Applicants
(212) 408-2627

Baker Botts LLP
30 Rockefeller Plaza
New York, New York 10112

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

The following claims have been **amended** as follows:

1. (Amended) An expression vector comprising a vaccinia virus [having] with reduced pathogenicity in an animal host which comprises an E3L gene having a deletion of the region encoding amino acids 184-190 of the E3L gene product wherein said vector further comprises exogenous DNA operably linked to regulatory elements that control expression of said exogenous DNA.

5. (Amended) A method of making a recombinant gene product comprising subjecting an expression vector comprising a vaccinia virus [having] with reduced pathogenicity in an animal host which comprises an E3L gene having a deletion of the region encoding amino acids 184-190 of the E3L gene product and wherein said vector further comprises exogenous DNA that encodes said recombinant gene product operably linked to regulatory elements that control expression thereof, to conditions whereby said recombinant gene product is expressed.

The following new claim has been **added**:

7. (New) A method of inducing a protective immune response in a subject comprising introducing to the subject an expression vector comprising vaccinia virus with reduced pathogenicity in an animal host which comprises a E3L gene having a deletion of the region encoding amino acids 184-190 of the E3L gene product wherein said vector further comprises

exogenous DNA operably linked to regulatory elements that control expression of said exogenous DNA.